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(71) Applicant
Akademie der Wissenschaften der DDR (DR Germany), Rudower Chaussee 5, DDR-1199 Berlin, German Democratic Republic

(72) Inventors
Horst Dautzenberg,
Fritz Loth,
Klaus Pommerening,
Karl-Joachim Linow,
Dieter Bartsch

(74) Agent and/or Address for service
Venner Shipley & Co.,
368 City Road, London EC1V 2QA

(54) Microcapsules and process for the production thereof

(57) The present invention provides microcapsules with a semipermeable or permeable capsule wall and a liquid core, wherein the capsule wall consists of a polyelectrolyte complex formed from counter-charged polyelectrolytes or from polyelectrolyte and low molecular weight organic counter ions and the liquid core consists of an aqueous solution of a polyelectrolyte.

A process for the production of microcapsules with a semipermeable or permeable wall for the encapsulation of dissolved, emulsified or suspended substances, comprises introducing an aqueous solution of a polyelectrolyte in the form of preformed particles into an aqueous solution of a counter-charged polyelectrolyte or of a counter-charged low molecular weight organic compound as a precipitation bath.

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SPECIFICATION

Microcapsules and process for the production thereof

The present invention is concerned with microcapsules with a semipermeable or permeable capsule wall and a liquid core and with a process for the production thereof.

According to the process of the present invention, sensitive substances can be encapsulated under physiological conditions. The products hereby obtained can be used, for example, for separating and substance-converting processes in preparative and analytical chemistry and biochemistry, in pharmacy and in medicine, as well as for agricultural and foodstuff purposes.

Microcapsules with a semipermeable or permeable capsule wall and a liquid core are known in a large variety of different forms (see V.D. Solodivnik, Mikrokapselung, Chimija, Moscow, 1980; J.R. Nixon, Microencapsulation, Marcel Dekker Inc., New York and Basel, 1976; J.E. Vandegaer, Microencapsulation Processes and Applications, Plenum Press, New York and London, 1974; M. Gulcho, Capsule Technology and Microencapsulation, Noyes Data Corp., Park Ridge, 1972).

However, the polymers or polymer combinations used for the capsule walls have, in many cases, disadvantages with regard to their permeation properties, their elasticity and their mechanical stability, for example, in the case of a high osmotic pressure within the capsule. In most cases, the liquid core consists of an oily, water-immiscible organic liquid which has a disadvantageous effect on the properties of substances to be encapsulated and upon the substance transport in the case of the use of the microcapsules in aqueous systems.

Numerous mechanical-physical and chemical processes are known for the production of microcapsules. Th principle of the mechanical-physical encapsulation process consists, in general, in that the core material is sprayed and enclosed in a gas chamber with the wall material. The wall material can thereby be already dissolved in the core material (spray drying) or subsequently brought into contact with the core material particles or droplets (dip process, multi-material spray process, fluidised bed coating and the like). The disadvantages of these processes are, in particular, the use of comparatively high temperatures, the use of organic solvents or the impermeability of the capsule covering The chemical processes are mostly carried out in the liquid phase, the wall formation taking place by boundary surface polymerisation or condensation or by deposition of a particular polymeric wall material. The use of mostly aggressive monomers and organic solvents is an important disadvantage of the encapsulation process by boundary surface reactions.

In the case of the chemical processes with the use of a particular polymeric wall material, it is a common feature of most of them that the core material is emulsified or suspended in the continuous phase and the polymer dissolved in the continuous phase is precipitated out on the phase boundary between the core and the continuum, for example by changing the pH value or the temperature, adding salts or solvents or the like. In the case of the encapsulation of sensitive materials, such onditions easily result in damage thereof.

In the case of the frequently employed complex coacervation, precipitating out of the wall material takes place by two counter-charged polymers (see W. Sliwka, Angew. Chem., *87*, 556-567/1975).

The use of water-immiscible organic liquids as core material and the usually necessary solidification of the capsule wall, for which, in some cases, really very drastic reaction conditions are necessary, are the most important disadvantages of this process.

A relatively mild enclosure process consists in the production of mixtures of the material to be encapsulated with an aqueous polyelectrolyte solution and introduction of this mixture into a precipitation bath containing a low molecular weight ion. As a result of ion diffusion, form-stable bodies thereby result with a permeable gel meshwork (see J. Klein, U. Hackel, P. Schara and H. Eng, Angew. Makromol. Chem., *76/77*, 329-350/1977 and Federal Republic of Germany Patent Specification No.1,917,738).

As a result of the necessary pH changes and/or the presence of polyvalent metal ions, this process also results in a partial damage of sensitive materials. Furthermore, such meshworks do not possess a permeable or semi-permeable capsule wall and a liquid core.

Federal Republic of Germany Patent Specification No. 3,012,233 describes a further developed process, starting from such gel particles, for the immobilisation of sensitive biological systems in which pearl-shaped particles are, by subsequent treatment with an appropriate polyelectrolyte solution, covered with a polyelectrolyte complex membrane and the gel is again liquefied by ion exchange with appropriate buffer solutions. The microcapsules hereby obtained suffer from the disadvantage that, in the case of production and handling, they are very sensitive towards external influences since the capsule walls have only a very low mechanical strength. The process also does not exclude the possibility of a damaging influence of polyvalent metal ions. Furthermore, the necessary reliquefaction of the gel core by ion exchange represents an additional engagement into the whole system.

It is an object of the present invention to provide microcapsules with improved properties and a process for the production thereof, in order to provide new possibilities with regard to the encapsulation of sensitive substances and new fields of use for the products obtained.

Therefore, the problem with which the present invention is concerned is to provide microcapsules and a process for the production thereof in which, at the same time, the encapsulation of sensitive substances can be ensured. The microcapsule production must thereby be capable of being carried out under as gentle conditions as possible. for example under physiological conditions, and the capsule wall must be an elastic, permeable or semi-permeable membrance which has a sufficient stability towards chemic-

al influences and mechanical stresses. The interior of the capsule is to be liquid and must not give rise to any damage to the substance to be encapsulated.

Thus, according to the present invention, there are provided microcapsules with a semipermeable or permeable capsule wall and a liquid core, wherein the capsule wall consists of a polyelectrolyte complex formed from counter-charged polyelectrolytes or from polyelectrolyte and low molecular weight organic counter ions and the liquid core consists of an aqueous solution of a polyelectrolyte.

For the production of the microcapsules according to the present invention, the aqueous solution to be encapsuled of a polyelectrolyte is introduced in the form of pre-formed and preferably spheroidal particles into an aqueous solution of a counter-charged low molecular weight organic compound as precipitation bath.

A substance to be encapsulated can thereby be contained in the solution of the polyelectrolyte used as core material. By mutual precipitating out of the counter-charged polyelectrolyte components or of the polyelectrolyte with the counter-charged low molecular weight organic compound, on the contact surface of both solutions there is immediately formed an insoluble membrance consisting of the corresponding polyelectrolyte complex which membrane envelops the substance to be encapsulated, which is present in the core material.

In the case of the process according to the present invention, this covering is a membrane which is impermeable to dissolved high molecular weight compounds but is very thin and mechanically stable, the membrane encompassing the polyelectrolyte solution used as core material and the substance possibly to be encapsulated. Important for the formation and the properties of the membrane cover formed are the nature of the polyelectrolytes used or of the low molecular weight organic ions, the precipitation conditions, the concentration ratios in the boundary layer and the viscosity of the solution used as core material. We have found that the thickness of the capsule wall can be controlled in a radial direction to the interior of the capsule by differing residence times of the polyelectrolyte solution droplets in the precipitation bath. The encapsulation conditions can be varied within wide limits with regard to the temperature and pH value of the polyelectrolyte solutions but, for the most gentle encapsulation possible of sensitive substances, temperatures of from 273 to 323°K and pH values of from 5 to 9 are preferred.

As solvent for the particular polyelectrolyte components or for the low molecular weight organic ions, use can be made of pure water.

The use of buffer mixtures, for example 0.001 to 1M phosphate buffer, or of solutions of low molecular weight electrolytes makes possible, in addition, the aimed for adjustment of particular pH values and of differing ionic strengths. With regard to the polyelectrolytes used according to the present invention for the core material, there have proved useful sulphate- and carboxylate group-containing polysaccharides and polysaccharide derivatives, for example cellulose sulphate. dextran sulphate, starch sulphate, cellulose acetate sulphate, carboxymethylcellulose sulphate, carboxymethylcellulose and alginates, in the form of their sodium salts, individually or as mixtures. However, there can also be used carboxylate or sulphonate group-containing synthetic polymers, for example poly- or copolyacrylates and maleates and polystyrene sulphonate. The polyelectrolyte concentration in the aqueous core material can be varied, depending upon the nature of the polyelectrolyte employed and the degree of polymerisation, between 0.5 and 20% by weight and preferably between 1 and 10% by weight.

Whereas the degree of substitution of the polysaccharide sulphate or carboxylate can be varied within wide limits, for example from 0.3 to 2.5, the degree of polymerisation should not be too low since a certain minimum viscosity is necessary for the stability of the microcapsules at the stage of formation. The viscosity of the finished core material mixture should preferably be kept within the limits of from 0.1 to 10 Pa.s and be 10 to 100 times the viscosity of the precipitation bath. The viscosity of the core material mixture can be controlled not only via the concentration and the degree of polymerisation of the polyelectrolyte employed but also by the addition of other appropriate water-soluble polymers.

According to the present invention, for the precipitation bath there can be used aqueous solutions of polycations with quaternary ammonium groups, for example polydimethyldiallylammonium chloride and polyvinylbenzyltrimethylammonium chloride, or of low molecular weight organic cations, especially cationic tensides and/or cationic coloured materials with a quaternary nitrogen grouping.

Of the cationic tensides, quaternary ammonium salts, for example lauryldimethylbenzylammonium chloride, pyridinium salts, for example stearamidomethylenepyridinium chloride, and imidazolium salts, for example heptadecylimidazolium chloride, have proved to be especially preferable. The hydrophilic long-chained alkyl or arylalkyl radicals of the tensides can be interrupted by heteroatoms or heteroatom groups, for example d iisobutylphenylethoxyethyldimethylbenzylammonium chloride or dodecylcarbamylmethylbenzyldimethylammonium chloride.

As cationic colouring materials, there can be used, for example, aminotriarylmethane dyestuffs, acridine dyestuffs, methine dyestuffs, phenazine dyestuffs, thiazine dyestuffs, oxazine dyestuffs or azo dyestuffs. The concentration of polycation, cationic tenside and/or cationic dyestuff in the precipitation bath should preferably be from 0.1 to 20% by weight and more preferably from 0.2 to 10% by weight.

The process according to the present invention is extremely simple to carry out. First, the aqueous polyelectrolyte solution intended for the core material is mixed at the optimum pH value for the substance to be encapsulated and at an appropriate temperature with the substance to be encapsulated, which can already be present as an aqueous solution, dispersion or in solid form. The mixture hereby obtained is now formed into spheroidal particles by simply allowing it to drop from a capillary or by

blowing with air or an inert gas the droplets forming, for example with the use of a concentric nozzle, the particles being introduced into the stirred or otherwise moved, possibly tempered and buffered precipitation bath. The formation of the capsule cover takes place immediately in the case of mutual contacting of the core material droplets and the precipitation bath. For this reason, the separation of the microcapsules formed can also be carried out directly after the introduction. However, it is advantageous to leave the microcapsules for from 10 seconds to 24 hours and preferably from 5 to 120 minutes or even longer in the precipitation bath. In this manner, the thickness of the wall layer and the properties thereof are also readily reproducible in the case of the same material and constant encapsulation conditions.

The wall thickness obtained is thereby of the order of magnitude of from 0.1 to 50μm. and preferably of from 1 to 20μm. In the case of the use of low molecular weight counter ions, it can, however, be substantially greater. The size of the microcapsules can be varied, by appropriate technical arrangement of the forming process and the viscosity of the core material, within the limits of from 50 to 5000μm. For the achievement of uniform, spheroidal microcapsules, between the outlet opening of the capillary or of the nozzle and the surface of the precipitation bath, there is maintained a distance of 5 to 200 cm. and preferably of 10 to 100 cm.

After the actual microencapsulation, there generally follows the separation of the microcapsules formed from the precipitation bath by filtration or decanting and rinsing off of excess, adhering precipitation bath with water or buffer solution.

For the solidification and for the lowering of the permeability of the capsule wall, there can also be carried out a treatment of the microcapsules with a dilute, for example 0.01 to 1% aqueous solution of the polyelectrolyte used as core material, after which there preferably follows another precipitation bath treatment.

The microcapsules according to the present invention are very stable with regard to deformation and increased osmotic pressure. However, in the case of too high a mechanical stressing, they burst and liberate the liquid capsule contents. They can be frozen without damage to the capsule wall taking place upon thawing again. The capsule wall is also stable towards chemical influences, for example 0.1N aqueous sodium hydroxide solution, 0.1N hydrochloric acid, ethanol and acetone. For low molecular weight inorganic and organic substances, for example protons, hydroxyl ions, water, dissolved salts, dyestuffs and sugars, the membrance does not represent a substantial diffusion barrier.

The following Examples are given for the purpose of illustrating the present invention:

Example 1

0.5 g. Sodium cellulose sulphate with a degree of substitution of 2.0 is dissolved in 10 ml. 0.01N phosphate buffer (pH 7.0). The solution obtained is forced at ambient temperature through a capillary with an inner diameter of 0.2 mm. and, after a falling distance of 30 cm., introduced into a stirred precipitation bath of 2 g. polydimethyldiallylammonium chloride (relative molecular weight 40,000) and 100 m1. 0.01M phosphate buffer (pH 7.0). Immediately after entry into the precipitation bath, the droplets become covered with a skin of a complex of the two counter-charged polyelectrolytes. After 30 minutes, the microcapsules obtained are separated by decanting from the precipitation bath and washed with 0.01N phosphate buffer (pH 7.0). The spheroidal microcapsules have a diameter of 2 to 3mm., are transparent and contain, as core material, the cellulose sulphate solution used.

The capsule wall formed is free of defects and is a membrance which is permeable to low molecular weight substances. If the microcapsules are suspended in a 0.01N aqueous sodium hydroxide solution coloured with phenolphthalein and the suspension medium is decolorised after about 3 minutes with 0.1N hydrochloric acid, then the capsules maintain their red colour for a few minutes and then slowly decolorise. In the case of adding salt to the suspension medium, the particles first shrink with deformation. Upon subsequently washing with water, they again assume their spheroidal shape.

Example 2

0.2 g. Sodium cellulose sulphate with a degree of substitution of 0.3 is dissolved in 10 ml. water. The solution obtained is forced through a capillary with an inner diameter of 0.2 mm. and blown out via a concentric nozzle with the help of a current of nitrogen in such a manner that individual liquid droplets with a diameter of 100 to 500 μm. result.

After a dropping distance of 15 cm., the spheroidal droplets are introduced into a stirred precipitation bath of 2g. polydimethyldiallylammonium chloride and 100 ml. water. Immediately after coming into contact with the precipitation bath, the droplets become coated with a skin of the complex formed of the two counter-charged polyelectrolytes. After 30 minutes, the microcapsules obtained are separated off from the precipitation bath by decanting and washed with water. There are obtained transparent, spheroidal particles with a diameter of 100 to 500 μm., the capsule wall of which has a thickness of from 1 to 5 μm.

Example 3

1.5 g. Sodium dextran sulphate with a degree of substitution of 0.8 is dissolved in 10 ml. water. The solution obtained is warmed to 277°K and, as in Example 1, introduced into a precipitation bath, also warmed to 277°K, consisting of 10g. polydimethyldiallylammonium chloride and 100 ml. water. After 60 minutes, the microcapsules formed are separated from the precipitation bath by decanting, mixed with 100 ml. of a 0.1% dextran sulphate solution, after 10 minutes separated off from the dextran sulphate solution and subsequently again treated for 30 minutes with the precipitation bath. Microcapsules are obtained with a diameter of 3 to 4 mm. and a wall thickness of about 20 μm.

Example 4

0.3 g. Sodium carboxymethylcellulose sulphate with a degree of substitution of carboxyl groups of 0.6 and of sulphate ester groups of 0.3 is dissolved in 10 ml. water. The solution obtained is warmed to 313°K and, as in Example 1, introduced into a precipitation bath,also warmed to 313°K, of 3 g. polyvinylbenzyltrimethylammonium chloride and 100 ml. water. After 60 minutes, the capsules are separated from the precipitation bath by decanting and washed with water. There are obtained transparent capsules with a diameter of about 3 mm.

Example 5

0.3 Sodium cellulose acetate sulphate are dissolved in 100 ml. water. The solution obtained is, as in Example 1, dropped into a precipitation bath which has been obtained by dissolving 3 g. polydimethyldiallylammonium chloride in 100 ml. dilute hydrochloric acid and has a pH value of 4. After 60 minutes, the capsules are separated from the precipitation bath by decanting and washed with water. There are obtained transparent microcapsules with a diameter of about 3 mm.

Example 6

0.3 g. Sodium polystyrene sulphonate is dissolved in 100 ml. water. The solution obtained is, as in Example 1, dropped into a precipitation bath of 3 g. polydimethyldiallyammonium chloride and 100 ml. water. After 30 minutes, the capsules are separated from the precipitation bath by decanting and washed with water. There are obtained whitish-turbid microcapsules with a diameter of about 2 mm. and a liquid core.

Example 7

0.2 g. Sodium cellulose sulphate with a degree of substitution of 0.4 is dissolved in 9.8 ml. water. The solution obtained is forced at ambient temperature through a capillary with an inner diameter of 0.2 mm. and, after a dropping distance of 30 cm., introduced into a precipitation bath of 1 g. methylene blue and 99 ml. water. Immediately after entry into the precipitation bath, the droplets become covered with a skin. After 30 minutes, the capsules formed are separated from the precipitation bath by decanting and washed with water. There are obtained deep blue-coloured spheroidal capsules with a diameter of 3 to 5 mm.

Example 8

0.3 g. Sodium carboxymethylcellulose with a degree of substitution of 0.6 is dissolved in 9.7 ml. water. The solution obtained is forced through a capillary with an inner diameter of 0.2 mm. and blown off via a concentric nozzle with the help of a current of nitrogen in such a manner that individual liquid droplets result with a diameter of 100 to 300 μm. The droplets are blown into a stirred precipitation bath of 2 g. dodecylcarbamylmethylbenzyldimethylammonium chloride and 98 ml. water. After 120 minutes, the microcapsules formed are separated off with the help of a fine polyamide sieve from the precipitation bath and throughly washed with water. There are obtained white, non-transparent spheroidal particles with a diameter of 100 to 300 μm.

Example 9

0.2 g. Sodium carbocymethylcellulose sulphate with a degree of substitution of carboxyl groups of 0.6 and of sulphate ester groups of 0.3 is dissolved in 9.8 g. water. The solution obtained is, as in Example 7, formed into spheroidal droplets and introduced into a precipitation bath of 1 g. crystal violet (C.I. Basic Violet 3) and 99 ml. water. After 10 minutes, the capsules formed are separated from the precipitation bath by decanting and thoroughly washed with water until the water remains colourless. The capsules are dark violet coloured and have a diameter of 3 to 5 mm.

Example 10

0.2 g. Sodium cellulose sulphate with a degree of substitution of 0.4 is dissolved in 9.8 ml water. The solution obtained is, as in Example 8, formed into spheroidal particles and introduced into a precipitation bath of 2 g. safranin (C.I. Basic Red 2) and 98 ml. water. After 30 minutes, the microcapsules are removed by means of a sieve from the precipitation bath and thoroughly washed with water. There are obtained dark red spheroidal particles with a diameter of 100 to 300 μm.

Example 11

0.2 g. Sodium alginate is dissolved in 9.8 ml. water and the solution formed, as in Example 7, into spheroidal particles. These are introduced into a stirred precipitation bath of 1 g, safranin (C.I. Basic Red 2), 1 g. polydimethyldiallylammonium chloride and 98 ml. water. After 60 minutes, the capsules are sieved off and washed with water. There are obtained dark red spehroidal particles with a diameter of 3 to 5 mm.

Example 12

0.2 g. Sodium cellulose sulphate with a degree of substition of 0.4 is dissolved in 9.8 ml. water, the solution obtained is, as in Example 7, forced through a capillary and dropped into a precipitation bath of 1 g. acridine orange (C.I. Basic Orange 14) and 99 ml. water. After 60 minutes, the capsules are sieved off and washed with water until the wash water runs off colourless. There are obtained strongly orange-coloured, spheroidal capsules with a diameter of 3 to 5 mm.

Example 13

0.2 g. Sodium polystyrene sulphonate is dissolved in 9.8 ml. water, the solution obtained is, as in Example 7, forced through a capillary and dropped into a precipitation bath of 2 g. benzethonium chloride and 98 ml. water. After 2 hours, the capsules formed are sieved off and thoroughly washed with water. There are obtained white, non-transparent spheroidal particles with a diameter of 3 to 5 mm.

Example 14

0.2 g. Sodium cellulose sulphate is dissolved in 9.8 ml. water, the solution, as in Example 7, is forced

through a capillary and dropped into a precipitation bath of 2 g. lauryldimethylbenzylammonium chloride and 98 ml. water. After 2 hours, the capsules formed are sieved off and thoroughly washed with water. There are obtained white, non-transparent spheroidal particles with a diameter of 3 to 5mm.

CLAIMS

1. Microcapsules with a semipermeable or permeable capsule wall and a liquid core, wherein the capsule wall consists of a poluelectrolyte complex formed from counter-charged polyelectrolytes or from polyelectrolyte and low molecular weight organic counter ions and the liquid core consists of an aqueous solution of a polyelectrolyte.

2. Microcapsules according to claim 1, wherein the capsule wall consists of a complex of sulphate group-containing polysaccharides or polusaccharide derivatives or of sulphonate group-containing synthetic polymers and polymers with quaternary ammonium groups and the liquid core consists of the aqueous solution of the sulphate group-containing polysaccharide or polysaccharide derivative or sulphonate group-containing synthetic polymer used for the formation of the capsule wall.

3. Microcapsules according to claim 1, wherein the capsule wall consists of a complex of sulphate or carboxylate group-containing polysaccharides or polysaccharide derivatives or sulphonate or carboxylate group-containing synthetic polymers and cationic tensides or the cationic dyestuffs and the liquid core consists of the aqueous solution of the sulphate or carboxylate group-containing polysaccharides or polysaccharide derivative or sulphonate or carboxylate group-containing synthetic polymer used for the capsule wall formation.

4. Microcapsules according to claim 2 or 3, wherein the sulphate group-containing polysaccharide or polysaccharide derivative is cellulose sulphate, cellulose acetate sulphate, carboxymethylcellulose sulphate, dextran sulphate or starch sulphate in the form of a sodium salt.

5. Microcapsules according to any claims 2 to 4, wherein the degree of substitution of the sulphate group-containing polysaccharide or polysaccharide derivative is 0.3 to 2.5 with regard to the sulphate ester groups.

6. Microcapsules according to claim 2 or 3, wherein the sulphonate group-containing synthetic polymer is sodium polystyrene sulphonate.

7. Microcapsules according to claim 2 or 3, wherein the carboxylate group-containing polysaccharide or polysaccharide derivative is carboxymethylcellulose, carboxymethylcellulose sulphate or alginate in the form of a sodium salt.

8. Microcapsules according to claim 2, wherein the polymer with quaternary ammonium groups is polydimethyldiallyammonium chloride or polyvinylbenzyl-trimethylammonium chloride.

9. Microcapsules according to claim 3, wherein the cationic tenside is a quaternary ammonium, pyridinium or imidazolium salt and the cationic dyestuff is an aminotriarylmethane dyestuff, an acridine dyestuff, a methine dyestuff, a phenazine dyestuff, a thiazine dyestuff, an oxazine dyestuff or an azo dyestuff.

10. Microcapsules according to any of the preceding claims, wherein the capsules have an outer diameter of 50 to 5000μm.

11. Microcapsules according to any of the preceding claims, wherein the capsule wall thickness is 0.1 to 50μm.

12. Microcapsules according to claim 11, wherein the capsule wall thickness is 1 to 20 μm.

13. Microcapsules according to any of the preceding claims, wherein the capsules contain further substances in dissolved, emulsified or suspended form.

14. Microcapsules according to claim 1, substantially as hereinbefore described and exemplified.

15. Process for the production of microcapsules with a semipermeable or permeable wall for the encapsulation of dissolved, emulsified or suspended substances, wherein an aqueous solution of a polyelectrolyte in the form of preformed particles is introduced into an aqueous solution of a counter-charged polyelectrolyte or of a counter-charged low molecular weight organic compound as a precipitation bath.

16. Process according to claim 15, wherein a substance to be encapsulated is added to the polyelectrolyte solution used as core material.

17. Process according to claim 15 or 16, wherein the particle formation takes place by dropping from a capillary.

18. Process according to claim 15 or 16, wherein the particle formation takes place by spraying.

19. Process according to any of claims 15 to 18, wherein the preformed particles traverse a distance of 5 to 200 cm. to the surface of the precipitation bath.

20. Process according to claim 19, wherein the preformed particles traverse a distance of 10 to 100 cm. to the surface of the precipitation bath.

21. Process according to any of claims 15 to 20, wherein the concentration of the polyelectrolyte solution used as core material is from 0.5 to 20% by weight.

22. Process according to claim 21, wherein the concentration of the polyelectrolyte solution used as core material is from 1 to 10% by weight.

23. Process according to any of claims 15 to 22, wherein the concentration of polyelectrolyte or low molecular weight organic counter ion in the precipitation bath is from 0.1 to 20% by weight.

24. Process according to claim 23, wherein the concentration of polyelectrolyte or low molecular weight organic counter ion in the precipitation bath is from 0.2 to 10% by weight.

25. Process according to any of claims 15 to 24, wherein the solvent used for the polyelectrolyte or for polyelectrolyte and low molecular weight counter ion is water of a 0.001 to 1 molar aqueous solution of low molecular weight electrolyte.

26. Process according to claim 25, wherein the aqueous solution of low molecular weight electrolyte is a buffer solution.

27. Process according to any of claims 15 to 26, wherein the encapsulation takes place at a pH of

from 5 to 9.

28. Process according to any of claims 15 to 27, wherein the microcapsules formed are left in the precipitation bath for from 10 seconds to 24 hours.

29. Process according to claim 28, wherein the microcapsules formed are left in the precipitation bath for from 5 to 120 minutes.

30. Process according to any of claims 15 to 29, wherein the microcapsules formed are left in the precipitation bath at a temperature of from 273 to 323°K.

31. Process according to claim 15 for the production of microcapsules, substantially as hereinbefore described and exemplified.

32. Microcapsules, whenever produced by the process according to any of claims 15 to 31.

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